

Attorney Docket No. 52003-8001.US01

Amendments to the Specification:

Replace the paragraph on page 19, lines 6-9 with the following:

A discriminator [[42]] in the apparatus, also forming part of computer 28, functions to discriminate PREs with a selected spectral signature, i.e., a selected range of values of one or more selected spectral emission characteristics, from other light-scattering entities in the computer image. Examples of the operation of the discriminator will be given below.

Replace the paragraph on page 21, lines 7-11 with the following:

Light reflected from the mirror may in turn be refracted or reflected [[(by)]] by a suitable circular lens element 50, fixed to the objective lens mount into a hollow cone of incident light 52, converging toward a focus at the sample plane of the target. As previously noted, the specular reflection of such rays causes them to return along the lines of the incident cone trajectories, where they are ultimately absorbed or otherwise removed from the optical system.

Replace the paragraph on page 21, lines 12-18 with the following:

In this darkfield system illustrated in Fig. 3, the angle between the optic axis and the incident rays illuminating the sample is larger than the largest angle between the optic axis and the rays scattered by the PREs which is accepted into the objective lens element 45, which is illustrated to be of the refractive form. Also incorporated in the total optical microscope, although not shown, is the ability to divert the light rays away from detector [[38]] 58 to other ports whereby the image may be observed visually through standard binocular eyepieces, or to yet another port, for example, for photographing the illuminated field.

Attorney Docket No. 52003-8001.US01

Replace the paragraph on page 21, lines 19-24 with the following:

It has been found to be suitable to use a Nikon DF/BF lens model CF Plan BD ELWD with magnification 100X and numerical aperture (N.A.) 0.8 as the lens system [[54]] 36, and also a model CF Plan BD ELWD with magnification 20X and N.A. 0.4. In that case, the rays entering the objective element of the lens may be rendered parallel and incident upon the 50% mirror 38, and into a relay lens 56 (typically magnification of 2X or 5X) that focus the rays to an image plane on detector (image capture device) [[58]] 38, where the detection is performed by a suitable CCD camera system.

Replace the paragraph on page 22, lines 24-29 with the following:

Thus, for example, to discriminate PREs with a selected spectral peak wavelength and peak width at half intensity, the computer image generated could provide a matrix of all field regions and the associated spectral peak wavelength and width values. The discriminator would then [[selected]] select those regions containing PREs whose spectral signature meets certain ranges of these two spectral emission values. Depending on the particular values chosen, the discriminator could classify light-scattering entities in the field in a number of ways, including distinguishing:

Replace the paragraph on page 23, lines 1-9 with the following:

In each case, the basis for the discrimination may be based on detected values, for each light-scattering entity in the field, of peak position, peak intensity, or peak width at half intensity of the spectral emission curve, peak halfwidth in the image plane, and polarization or angle of incidence response. Other spectral characteristics mentioned above are also contemplated. In particular, where the PREs have surface-localized fluorescent molecules or Raman-active molecular entities, the detecting may include detecting plasmon-resonance induced fluorescent emission or Raman spectroscopy emission from one or more of said molecules or entities, respectively, and these values are used as a basis of discriminating such PREs from other light-

Attorney Docket No. 52003-8001.US01

scattering entities. Fig. 11 shows a typical Raman spectrum of a Raman-active molecule carried on the surface of a PRE.

Replace the paragraph on page 52, lines 8-18 with the following:

The presence of specific substances of interest or other perturbations in a sample being tested may therefore be detected by noting the spectral response of PREs to substances which interact with the PREs. For example, a suitable sample can be prepared having PRE bound to a substrate. Selected molecules may be bound to the PRE surface. The optical scattering parameters (intensity, polarization dependence, angular dependence, wavelength dependence, etc.) of each such PRE are recorded. The sample is then treated with material which includes molecules of interest that selectively bind to the surface of the PRE in such a manner that after initial treatment and/or subsequent further treatments, the PRE scattering parameters have changed, confirming the local absorption of additional material or desorption of the additional or initial material, or other changes in the local dielectric environment. It can be appreciated that the initial PRE sample may be prepared as a test "library" or used to screen an "applied " library of proteins, antibodies, etc. These peak shifts and intensity changes can also be used to detect molecular perturbations such as association and dissociation due to changes in the PRE local dielectric environment.

Replace the paragraph on page 52, lines 20-22 with the following:

(D) Shift in Fluorescence Spectrum

~~shifts and intensity changes can also be used to detect molecular perturbations such as association and dissociation due to changes in the PRE local dielectric environment.~~